Remarks/Arguments

Claims 1-18, 32-39 and 45-70 were originally pending. Claims 19-31 and 40-44 were previously canceled. Claims 8, 10, 11, 12, 32-39 and 45-70 were withdrawn from consideration due to a restriction requirement and have now been cancelled. Claims 1-9 and 13-15 were rejected. Claims 4 and 8 have now been canceled. Claims 1 and 9 has been amended. Applicant asks that all pending claims be examined and allowed.

Objection To The Specification

The Examiner has objected to the Applicant's specification due to an embedded hyperlink. The specification has been amended to remove the reference to the embedded hyperlink. The Applicant's have also updated the application priority information.

Claim Objection

The Examiner has objected to the Applicant's claims. In particular, the Examiner has objected to Claim 9 due to improper dependency. Claim 9 has been amended to correct this oversight. Claim 4 was objected to due to improper dependency. Claim 4 has been canceled thus rendering the Examiner's objection moot. Claim 9 was objected to as failing to further limit the subject matter of Claim 1. The Applicant's respectfully disagree. As the Examiner points out, Claim 1 recites "wherein examining the ductal fluid sample to determine the presence of precancerous or cancerous ductal epithelial cells" and Claim 9 recites "wherein examining the ductal fluid comprises detection of an estrogen receptor in the ductal epithelial cells." Claim 9

clearly limits the method to the detection of ductal epithelial cells that have an estrogen receptor. Claim 1 describes a method for the detection of precancerous or cancerous ductal epithelial cells (with or without estrogen receptors). Since Claim 9 describes a subset of cells described in Claim 1, it is clear that Claim 9 further limits the subject matter of Claim 1.

For the reasons stated above, the Applicant's respectfully request the objections to the claims be withdrawn.

The Rejections Under 35 U.S.C. §112, Second Paragraph Should be Withdrawn

The Examiner has rejected claims 1 and 5 under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant's regard as the invention. The Examiner states that Claim 1 is indefinite because the phrase "or therapeutic treatment of breast cancer" is missing at the end of the claim. Although the Applicant's feel this phrase is redundant, the Applicant has added the entire phrase from the preamble "for risk reduction or therapeutic treatment of breast cancer." The Examiner has also rejected Claim 5 as being indefinite because "...it is unclear whether the sample is obtained from the same patient or from any patient or subject." The Applicant's traverse this rejection. The Applicant's would argue that it is axiomatic that in order to identify patients who have a likelihood of benefiting from the administration of an estrogen activity modulator for risk reduction or therapeutic treatment of breast cancer, one would examine the patient's own ductal fluid sample. The suggestion that the examination of other patient's ductal fluid samples to determine whether or not a completely different patient would benefit from the administration of an estrogen activity modulator without first examining the patient's own ductal fluid sample is

nonsensical. For the reasons stated above, the Applicant's respectfully request the rejections under 35 U.S.C. 112, second paragraph be withdrawn.

The Rejections Under 35 U.S.C. §102(b) Should be Withdrawn

The Examiner has rejected claims 1-4, 8, 9, and 13-15 under 35 U.S.C. 102(b) as being anticipated by Fabian *et al.* (J. Cell Biochem., 1993, 17G: 153-160, IDS). The Examiner states that Fabian *et al.* teaches a method of providing and cytologically examining ductal fluid obtained via fine needle aspiration from high and low risk women, wherein high risk women include those with first degree relative with breast cancer. The Applicants respectfully disagree.

The present invention teaches a method for identifying asymptomatic patients who have a likelihood of benefiting from the administration of an estrogen activity modulator for risk reduction or therapeutic treatment of breast cancer by providing a ductal fluid sample from at least one duct of a breast of the patient and examining the ductal fluid sample to determine the presence of precancerous or cancerous ductal epithelial cells. The specification describes two methods for retrieving ductal fluid from a patient's breast (page 5; first paragraph). One method is via a procedure called nipple aspiration and the other method is called ductal lavage which was pioneered by the Applicants. Both methods described by the Applicants are relatively non-invasive techniques by which ductal fluid is obtain by either applying suction to the nipple of a patient (nipple aspiration) or by inserting a smaller catheter into individual breast ducts.

Fabian *et al.* does not teach or suggest a method of obtaining ductal fluid from a patient. Fabian *et al.* teaches a method of obtaining ductal cells by use of fine needle aspiration. Fine needle aspiration is an invasive technique by which a needle is inserted through a patient's breast

and, in the present case, into the tissue behind the nipple in an attempt to sample terminal ducts (page 2; left column; third paragraph). No ductal fluid was sampled by the method of Fabian *et al.* To establish a case of *prima facie* anticipation, the single reference cited by the Examiner must describe and enable the claimed invention, including all claim limitations, with sufficient clarity and detail to establish that the subject matter already existed in the prior art and that its existence was recognized by persons or ordinary skill in the field of the invention. (*Crown Operations Int. Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1375, 62 USPQ2d 1917, 1921 (Fed Cir. 1984)). Claim 1, as presently amended, teaches using a ductal fluid sample from at least one duct of a breast of the patient. Since Fabian *et al.* does not teach or suggest the use of a ductal fluid sample, Fabian *et al.* cannot anticipate the claims of the present invention. For this reason, the Applicant's respectfully request the rejections under 35 U.S.C. 102(b), be withdrawn.

The Examiner has rejected claims 1-6, 8, and 13-15 under 35 U.S.C. 102(b) as being anticipated by Sauter *et al.* (British J. Cancer., 1997, 76(4): 494-501, IDS). The Examiner states that Sauter *et al.* teaches a non-invasive method for the early detection of breast cancer comprising collecting nipple aspirate fluid from a patient, cytologically analyzing the fluid, and evaluating the promising cancer markers. The Examiner then goes on to argue that since all the "active steps" of the claimed method are taught by Sauter *et al.*, the method of Sauter *et al.* would therefore be capable of identifying patients who have a likelihood of benefiting from the administration of an estrogen antagonist for risk reduction or therapeutic treatment of breast cancer (page 11). The Examiner lastly argues that the last sentence of the claim (i.e., wherein patients determined to have the presence of either precancerous or cancerous ductal epithelial

cells are considered likely to benefit from administration of an estrogen activity modulator" is not given patentable weight. The Applicants respectfully disagree.

In *Griffin v. Bertina* (285 F.3d 1029, 62 USPQ2d 1431 (Fed Cir. 2002)), the Federal Circuit held that the "wherein" clause was indeed a limitation of a claim and should be given patentable weight. Thus, in light of the last sentence of the claim being a limitation and the Examiner's indirect admission that Sauter *et al.* does not teach or suggest such a limitation, Sauter *et al.* therefore cannot anticipate the claims of the present invention. For this reason, the Applicant's respectfully request the rejections under 35 U.S.C. 102(b), be withdrawn.

The Examiner has rejected claims 1-4, 6-8, and 13-15 under 35 U.S.C. 102(b) as being anticipated by JAMA (May 7, 1973, 224 (6): 823-827) in view of Sauter *et al.* (British J. Cancer., 1997, 76(4): 494-501, IDS). The Examiner states that since all the "active steps" of the claimed method are taught by JAMA, the method of JAMA would therefore be capable of identifying patients who have a likelihood of benefiting from the administration of an estrogen antagonist for risk reduction or therapeutic treatment of breast cancer (page 13). As in Sauter *et al.*, the Examiner argues that the "wherein" clause of claim 1 is given no patentable weight. The Applicants respectfully disagree.

As mentioned previously, the Federal Circuit held that the "wherein" clause was indeed a limitation of a claim and should be given patentable weight. Thus, in light of the last sentence of the claim being a limitation and the Examiner's indirect admission that JAMA does not teach or suggest such a limitation, the method described in JAMA therefore cannot anticipate the claims of the present invention. For this reason, the Applicant's respectfully request the rejections under 35 U.S.C. 102(b), be withdrawn.

The Double Patenting Rejection Should be Withdrawn

Claims 1-8 and 15 have been rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 9, 13, 15, and 19-21 of USP 6,610,484. Application 10/608,225 and USP 6,610,484 were, at the time the invention of Application 10/608,225 was made, owned by Cytyc Corporation. For this reason, the Applicant's respectfully request the non-statutory obviousness-type double patenting rejection be withdrawn.

Claims 1, 4, 6-8 and 15 have been rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1, 2, 11, 13, and 22 of USP 6,642,009. Application 10/608,225 and USP 6,642,009 were, at the time the invention of Application 10/608,225 was made, owned by Cytyc Corporation.

For the reason mentioned above, the Applicants respectfully request the non-statutory obviousness-type double patenting rejections be withdrawn.

Conclusion

In light of the arguments presented above, Applicants respectfully submit that the claims are in condition for allowance. Early notice to this effect is solicited.

A one month extension of time is required, the formal request for which is attached but we do not believe that any fees for net addition of claims are required. However, in the event that additional fees for net addition of claims is required you are hereby authorized to be charged to Deposit Account No. 502855 referencing attorney docket number 12.003011.

Respectfully submitted,

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